An engineered cardiac reporter cell line identifies human embryonic stem cell-derived myocardial precursors.

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Funding Grants: Modeling Myocardial Therapy with Human Embryonic Stem Cells

Public Summary:
Unlike some organs, the heart is unable to repair itself after injury. Human embryonic stem cells (hESCs) grow and divide indefinitely while maintaining the potential to develop into many tissues of the body. We have identified heart stem cells derived from hESCs, and show that these human heart stem cells give rise to all of the different types of heart muscle found in the patients with heart disease. The identification of these heart stem cells will provide important insight into the pathways regulating human heart development, and provide a novel therapeutic reagent for the treatment of heart disease.

Scientific Abstract:
Unlike some organs, the heart is unable to repair itself after injury. Human embryonic stem cells (hESCs) grow and divide indefinitely while maintaining the potential to develop into many tissues of the body. As such, they provide an unprecedented opportunity to treat human diseases characterized by tissue loss. We have identified early myocardial precursors derived from hESCs (hMPs) using an alpha-myosin heavy chain (alphaMHC)-GFP reporter line. We have demonstrated by immunocytochemistry and quantitative real-time PCR (qPCR) that reporter activation is restricted to hESC-derived cardiomyocytes (CMs) differentiated in vitro, and that hMPs give rise exclusively to muscle in an in vivo teratoma formation assay. We also demonstrate that the reporter does not interfere with hESC genomic stability. Importantly, we show that hMPs give rise to atrial, ventricular and specialized conduction CM subtypes by qPCR and microelectrode array analysis. Expression profiling of hMPs over the course of differentiation implicate Wnt and transforming growth factor-beta signaling pathways in CM development. The identification of hMPs using this alphaMHC-GFP reporter line will provide important insight into the pathways regulating human myocardial development, and may provide a novel therapeutic reagent for the treatment of cardiac disease.